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1,2,4-Triazoles. II.[1] The Tautomerism of 3-α-Pyridyl-1,2,4-triazoline-5-thione and Its Methyl Derivatives

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Tautomerism of 3-α-pyridyl-1,2,4-triazoline-5-thione (I) and its methyl derivatives has been studied. The infrared spectra of these compounds indicated the presence of strong intermolecular hydrogen bonding in a solid state.

Comparison of the ultraviolet (UV) spectrum of 5-methylthio-3-α-pyridyl-1,2,4-triazole (II) with those of the fixed compounds revealed that II exists as 2*H*-5-methylthio-3-α-pyridyl-1,2,4-triazole both in ethanol and in cyclohexane. In the same way, it was found 1-, 2-, and 4-methyl-3-α-pyridyl-1,2,4-triazoline-5-thiones (III, IV, and V), which are capable of existing in thione-thiol tautomerism, exist in thione form in ethanol. The parent compound I was also found by means of UV spectroscopy to exist in the thione form of 1*H*,4*H*-3-α-pyridyl-1,2,4-triazoline-5-thione in ethanol.

In most publications, 1,2,4-triazoles have been represented by the structures which have a ring hydrogen atom at an arbitrary nitrogen atom of the triazole nulceus without clear evidence.[3–8] Atkinson and Polya suggested that whichever representation, mesomerism or tautomerism, was adopted, acidic hydrogen of 1,2,4-triazoles would not be shared equally between the three nitrogen atoms.[9]

Later, Potts explained the imino hydrogen atom of 1,2,4-triazoles was not attached to any of the nitrogen atoms, but rather existed as a charged atom closely bound by a negatively charged triazole nucleus stabilized by resonance.[10] However, Katritzky and Lagowski claimed that this interpretation was considered to be incorrect.[11] It has recently been shown from the ionization constants[12] and the nuclear magnetic resonance spectra[13] that 1*H* form is predominant in the tautomeric equillibrium of 1*H* and 4*H* forms of 1,2,4-triazole.

In the preceding report,[1] we reported the synthesis of 3-α-pyridyl-1,2,4-triazoline-5-thione (I) and its methyl derivatives. The present paper deals with a study of the tautomerism of these compounds which are capable of existing as several tautomeric forms. 3-Substituted 1,2,4-triazoles and 3,5-disubstituted 1,2,4-triazoles which have different substituents can exist in three tautomeric forms, since 1- and 2-positions of these triazoles are not equivalent.

5-Methylthio-3-α-pyridyl-1,2,4-triazole (II) can exist in the equillibrium of three tautomeric forms, IIa, IIb, and IIc, in which the ring hydrogen atom attached to the three different nitrogen atoms of the triazole ring.

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[1] Part I: S. Kubota, M. Uda, and M. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **19**, 2231 (1971).
[2] Location: *Shomachi, Tokushima.*
[3] E. Hoggarth, *J. Chem. Soc.*, **1949**, 1160.
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[12] W. Freiberg and C.F. Kröger, *Chimia*, **21** (4), 159 (1967).
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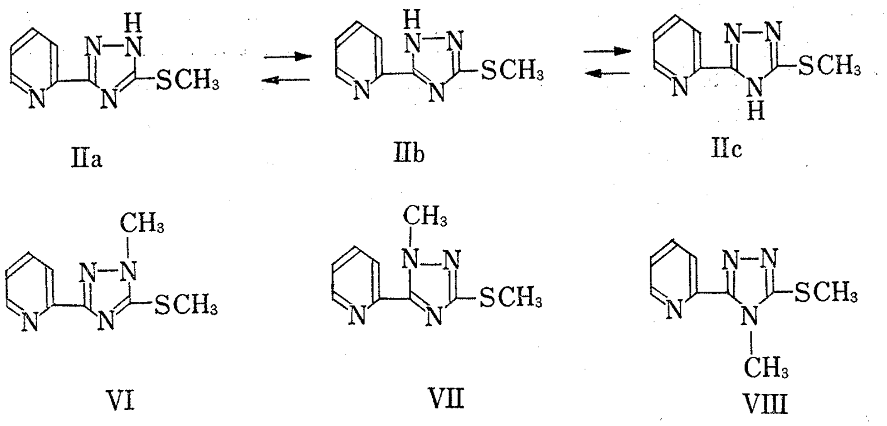

Chart 1

The infrared (IR) spectrum of II in KBr disk showed multiple combination bands in the 3300—2500 cm^{-1} region due to strong hydrogen bonding (Fig. 1b). In carbon tetrachloride, the intensity of these multiple bands decreased and that of another sharp NH band in the 3400 cm^{-1} region increased as the concentration of the solution decreased (Fig. 2). These spectral data suggested that II has intermolecular NH hydrogen bonds in a solid state.

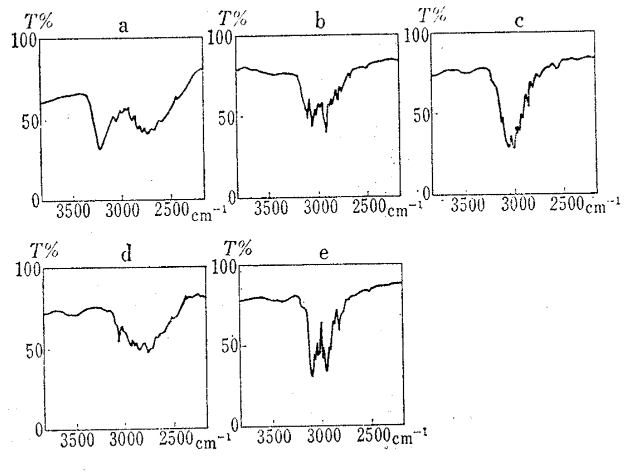

Fig. 1. Infrared Spectra in KBr Disk

a. 3-α-pyridyl-1,2,4-triazoline-5-thione (I)
b. 5-methylthio-3-α-pyridyl-1,2,4-triazole (II)
c. 1-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (III)
d. 2-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IV)
e. 4-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (V)

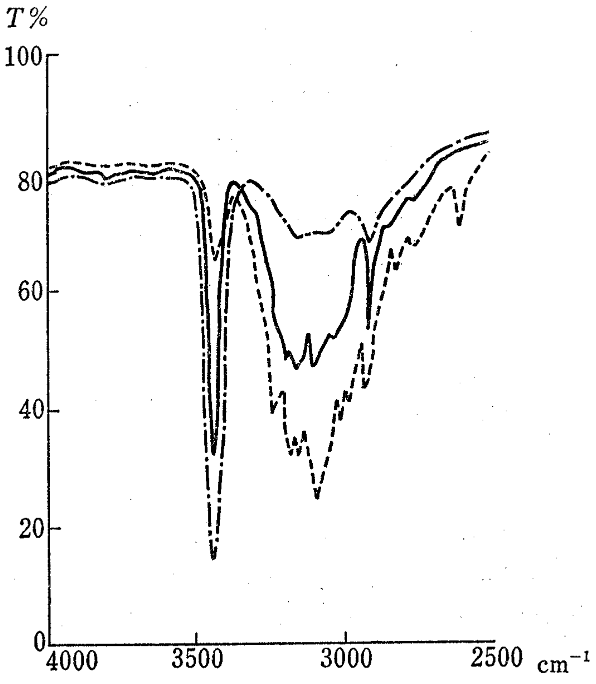

Fig. 2. NH-stretching Absorption Bands of 5-Methylthio-3-α-pyridyl-1,2,4-triazole (II) in Carbon Tetrachloride

—·—: 1×10^{-3}M ——: 1×10^{-2}M -------: 1×10^{-1}M

In a study of tautomerism of the alkyl derivative of 3-amino-5-(2-furyl)-1,2,4-triazole, Akerblom and Sandberg concluded these compounds exist predominantly in 2*H*-3-alkylamino- and 2*H*-3-dialkylamino-5-(2-furyl)-1,2,4-triazole from the fact that linear and cross conjugation between the furan and triazole rings shows different ring vibration bands in the 1500—1600 cm^{-1} region.[14]

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[14] E. Akerblom and M. Sandberg, *Acta Chem. Scand.*, **19**, 1191 (1965).

However, in the cases of compound I and its methyl derivatives, this method was unsuccessful since no significant difference could be found in the same region.

To study the tautomerism of II, the ultraviolet (UV) spectra of II both in ethanol and in cyclohexane were compared with those of the three *N*-methyl triazoles,[1] *i.e.*, 1-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VI), 2-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VII), and 4-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VIII) in the same solvents (Chart 1).

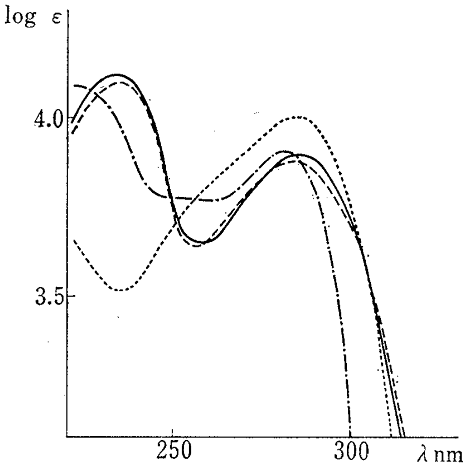


Fig. 3. Ultaviolet Spectra in Ethanol

——: 5-methylthio-3-α-pyridyl-1,2,4-triazole (II)
–·–: 1-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VI)
----: 2-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VII)
······: 4-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VIII)

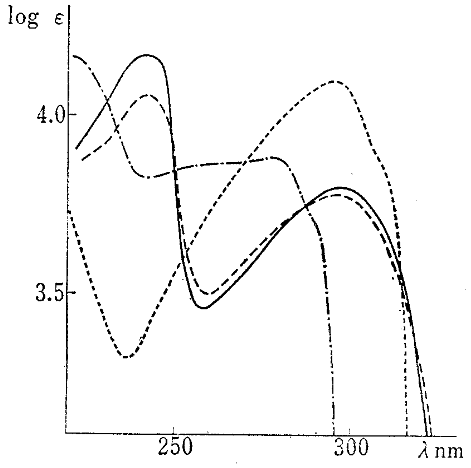


Fig. 4. Ultarviolet Spectra in Cyclohexane

——: 5-methylthio-3-α-pyridyl-1,2,4-triazole (II)
–·–: 1-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VI)
----: 2-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VII)
······: 4-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VIII)

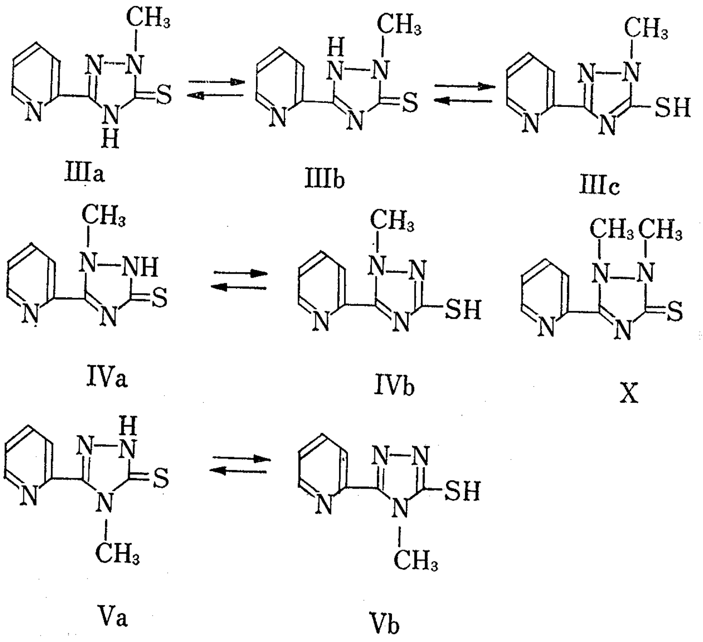


Chart 2

The UV spectra of VII and VIII showed absorption maxima at the longer wavelengths than that of VI, since VII and VIII have a linear conjugation while VI has a cross conjugation. The difference between the spectra of VII and VIII is explained by more extended conjugation of the latter involving S-methyl group (Fig. 3 and 4).

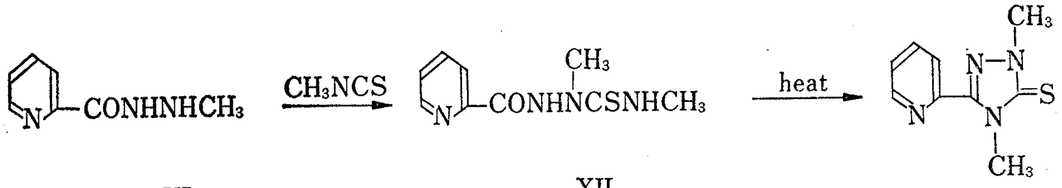
The UV spectrum of II showed absorption maxima at 235 nm and 286 nm in ethanol, at 241 nm and 297 nm in cyclohexane, respectively. These spectra were almost the same as those of VII, and different from those of VI or VIII both in ethanol and in cyclohexane (Fig. 3 and 4). From these UV spectral data, it was concluded that II is not represented as mesomerism but as tautomerism, and exists as 2*H*-5-methylthio-3-α-pyridyl-1,2,4-triazole (IIb) both in polar and in nonpolar solvents.

1-, 2-, and 4-Methyl-3-α-pyridyl-1,2,4-triazoline-5-thiones (III, IV, and V) can exist in thione-thiol tautomeric equillibria as shown in Chart 2.

The IR spectra of III, IV, and V in KBr disk showed characteristic broad fine structures in the 3000—2500 cm^{-1} region (Fig. 1c, d, and e).

These absorption bands indicated that these compounds contain the strong intermolecular hydrogen bonded NH groups in a solid state.

The UV spectra of III, IV, and V in ethanol were compared with those of VI, VII, VIII, and 1,4-dimethyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IX) in the same solvent. This compound IX was prepared by cyclization of 1-picolinoyl-2,4-dimethylthiosemicarbazide (XII) which was obtained from 1-picolinoyl-2-methylhydrazine (XI) and methylisothiocyanate.



XI XII IX

Chart 3

Compound III exhibited three absorption maxima at 221 nm, 252 nm, and 307 nm in ethanol. The spectrum of III was very similar to that of IX and showed the absorption maxima at considerably longer wavelength than that of VI, presumably due to chromophoric effect of the thiocarbonyl group. Therefore, the thione form of IIIa or IIIb type was assigned to III tentatively.

On the other hand, two tautomeric forms IVa and IVb are possible for IV. However, the spectrum of IV recorded in ethanol showed absorption maxima at 232 nm, 253 nm, and 277 nm and was greatly different from that of VII which is the model compound of IVb type.

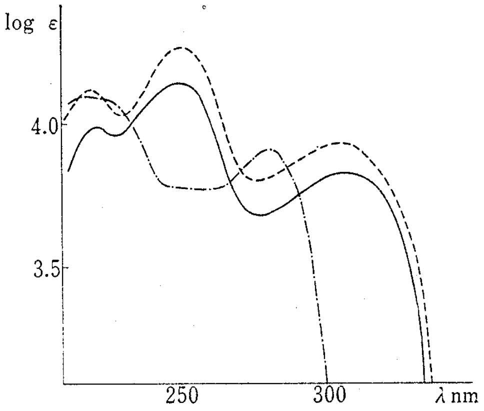


Fig. 5. Ultraviolet Spectra in Ethanol

——: 1-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (III)
-----: 1-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VI)
------: 1,4-dimethyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IX)

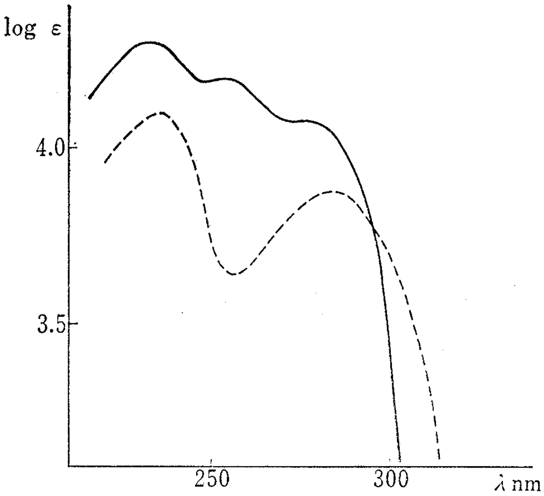


Fig. 6. Ultaviolet Spectra in Ethanol

——: 2-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IV)
------: 2-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VII)

From these spectral data, IV was considered to exist in thione form of IVa type, although the UV spectrum of IV could not be compared with that of 1,2-dimethyl-3-α-pyridyl-1,2,4-triazoline-5-thione (X) which is the model compound of IVa type since attempts to synthesize X were unsuccessful. The fact that the UV spectrum of compound III is very similar to that of IX which is the model compound of IIIa type, and greatly different from that of IV which is considered to show the same UV absorption as IIIb indicated that III exists predominantly in the thione form of IIIa type.

The thione-thiol tautomerism of Va—Vb can be considered for V. However, V exhibited three absorption maxima at 218 nm, 252 nm, and 301 nm in ethanol and the spectrum of V was almost the same as that of IX in the same solvent, while VIII, the model compound of Vb type, showed only a single peak at 284 nm. These UV spectral data supported that V exists in the thione form of Va type in ethanol.

Thus, it was found that all ring methylated compounds (III, IV, and V) exist in thione forms in ethanol. These results were in good agreement with the facts that some 1,2,4-triazoles capable of thione-thiol tautomerism exist predominantly in the thione forms.[15]

Compound I can exist in the tautomers of three thiol forms (Ia, Ib, and Ic types) and two thione forms (Id and Ie types) as shown in Chart 4.

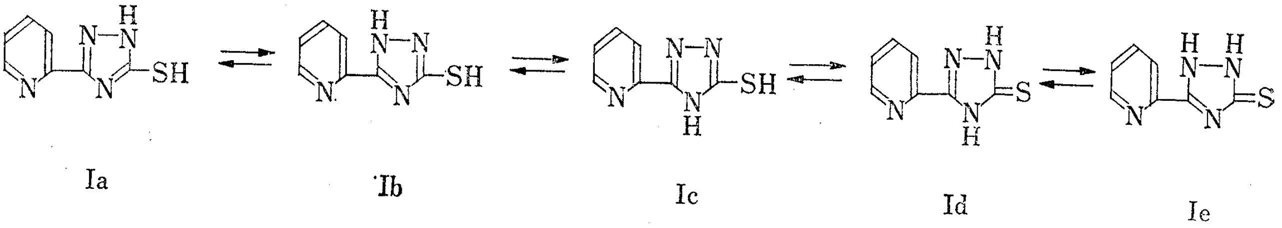


Chart 4

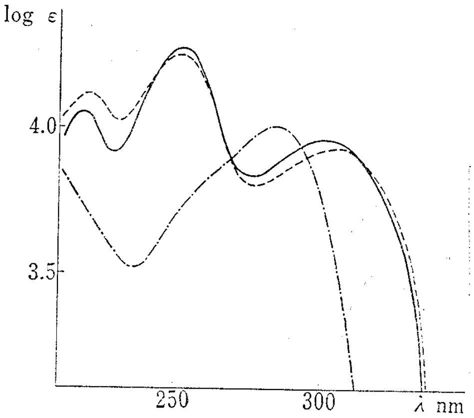


Fig. 7. Ultraviolet Spectra in Ethanol

——: 4-methyl-3-α-pyridyl-1,2,4-triazoline-5-thione (V)
-·-·-: 4-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VIII)
-----: 1,4-dimethyl-3-α-pyridyl1,2,4-triazoline-5-thione (IX)

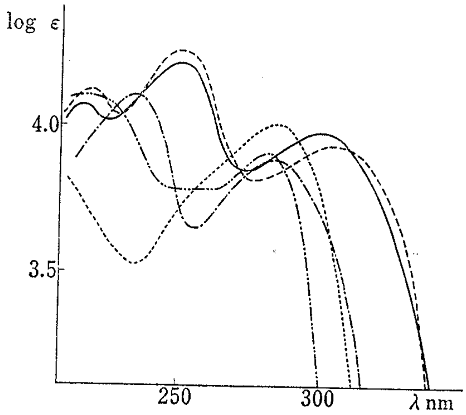


Fig. 8. Ultraviolet Spectra in Ethanol

——: 3-α-pyridyl-1,2,4-triazoline-5-thione (I)
-·-·-: 1-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VI)
-··-··: 2-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VII)
······: 4-methyl-5-methylthio-3-α-pyridyl-1,2,4-triazole (VIII)
-----: 1,4-dimethyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IX)

The IR spectrum of Compound I showed a broad absorption band of medium intensity in the 3200 cm^{-1} region with multiple combination bands extended to about 2200 cm^{-1} in a solid state (Fig. 1a). The broad absorption band appeard at higher frequencies can be assigned to the associated NH group. The characteristic multiple combination bands in lower frequencies were very similar to those of amine salt and suggested that the hydrogen atom of the imino group protonates a nitrogen atom of another molecule. The UV spectrum of I

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[15] A.J. Blackman and J.B. Polya, *J. Chem. Soc. (C)*, **1970**, 2403.

which has three absorption maxima at 218 nm, 250 nm, and 300 nm in ethanol was very similar to that of IX, the fixed methyl derivative of Id type and different from those of VI, VII, and VIII, the model compounds of Ia, Ib, and Ic types. These spectral data indicated that I exists predominantly in the thione form of Id type. This result is in accord with the conclusion reached on the basis of the nuclear magnetic resonance and IR spectra.[16)]

Experimental

IR and UV spectra were determined with Hitachi EPI-G_2 spectrophotometer and Hitachi model 124 spectrophotometer, respectively.

1-Picolinoyl-2,4-dimethylthiosemicarbazide (XII)——To a solution of 1.0 g of 1-picolinoyl-2-methylhydrazine (XI) in 5 ml of EtOH was added 1.0 g of methylisothiocyanate and the mixture was refluxed on a water bath for 30 min. After the mixture had been allowed to come to room temperature, the resulting precipitate was collected by filtration, washed with cold EtOH several times giving 1.2 g of colorless powder, mp 162—163°. *Anal.* Calcd. for $C_9H_{12}ON_4S$: C, 48.22; H, 5.40; N, 24.99. Found: C, 48.19; H, 5.61; N, 25.28.

1,4-Dimethyl-3-α-pyridyl-1,2,4-triazoline-5-thione (IX)——A solution of 0.9 g of in XII 1N NaOH was heated at 100° for 5 hr. After the mixture had been allowed to come to room temperature, the resulting precipitate was collected by filtration and recrystallized from EtOH to give colorless needles, 0.71 g, mp 144—145°. *Anal.* Calcd. for $C_9H_{10}N_4S$: C, 52.41; H, 4.89; N, 27.16. Found: C, 52.38; H, 5.02; N, 27.58.

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16) A.J. Blackman and J.B. Polya, *J. Chem. Soc.* (*C*), **1971**, 1016.